Docket No. SYRTECH 5001-U

### REMARKS/ARGUMENTS

## Rejection Under 35 USC 103(a)

The Examiner rejects claims 1-7, 16, 21-26, 31-36, 38, 40, 42, 45, 48 and 52-57 under 35 USC 103(a) on the grounds that the claims are rendered obvious over Kissinger, et al. (Acta Crystallographica Section D, Biological Crystallography, 1999, D44, 484-491).

In support of the Examiner's rejection, the Examiner states that "Kissinger discusses that instead of a single search model, a set of structural models that would compete in the evolutionary search process is a useful alternative and is preferable as it will greatly expand the range of applicability of MR." Applicants traverse the Examiner's broad reading of the last paragraph of column 2, page 490 of Kissinger and hence Examiner's support for the present rejection for obviousness.

For the sake of precision, the last paragraph of column 2, page 490 of Kissinger states:

Ultimately, it should be possible to incorporate not only optimization, but also selection of the search model into the procedure. Instead of a single search model, a set of structural models would be allowed to compete in the evolutionary search process. Although this will undoubtedly necessitate much larger population sizes and much longer computing times, early experiments suggest that this approach is feasible. When combined with a comprehensive database of protein structures, such a procedure could greatly expand the range of applicability of MR.

As Applicant will explain, for many reasons, this teaching is insufficient to render the claimed invention obvious.

(a) Kissinger is not enabling with regard to using multiple search models

<sup>1</sup> Examiner also rejects claim 49-51 but these claims are currently withdrawn.

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In order to be an effective prior art reference with regard to an obviousness rejection, Kissinger has to be enabling. By contrast, however, Kissinger does not teach how one would incorporate the use of multiple search models into the evolutionary algorithm procedure taught by Kissinger.

Applicant notes that Kissinger only states that "early experiments <u>suggest</u> that this approach is feasible" and fails to disclose how these early experiments were performed. Kissinger's own language suggests that Kissinger had <u>not</u> themselves actually reduced a process using multiple search models to practice. Thus, the teaching of Kissinger at best can be seen as a suggestion to try to extend the evolutionary algorithm procedure to multiple search models and fails to actually teach that the application of an evolutionary algorithm to multiple search models would work.

# (b) Kissinger's teaching is limited to using an evolutionary algorithm multiple search models

Kissinger, to the extent that it teaches the use of the method to select a search model, such teaching is limited to use of the evolutionary algorithm procedure taught by Kissinger. Specifically, Kissinger teaches that "it should be possible to incorporate not only optimization, but also selection of the search model <u>into the procedure</u>" and also teaches that "a set of structural models would be allowed <u>to compete in the evolutionary search process</u>." As noted above, Kissinger fails to teach how one would use an evolutionary algorithm to select among multiple search models.

It is noted that the pending claims do not use an evolutionary algorithm in order to select a search model. Rather, as stated in claim 1, the present invention

employ[s] computer executable logic to compare solutions from the multiple molecular replacement searches, the comparison producing data that predicts which biomolecule structures in the group have superior structural identity with the target biomolecule as compared to the other biomolecule structures in the group."

Claim 1,

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The process specified in claim 1 of comparing solutions from the multiple molecular replacement searches and then picking the best biomolecule structure to use as the search model is not an evolutionary process. Hence, even the non-enabled teaching of Kissinger does not render the claimed invention obvious.

### (c) Claimed invention provides unexpected results

As noted above, Kissinger teaches that the evolutionary algorithm procedure taught therein might be extendable to multiple search models and if extendable to multiple search models could greatly expand the range of applicability of molecular replacement. Kissinger thus fails to teach, let alone show, that the evolutionary algorithm procedure weakly suggested by Kissinger will be extendable to multiple search models and if extendable to multiple search models would greatly expand the range of applicability of molecular replacement. Applicants, by contrast, provide concrete experimental evidence that the claimed invention effectively enables one to pick the best search model from among multiple search models and does not require the use of an evolutionary algorithm anywhere in the process (although Applicant notes that nothing precludes one to follow the teaching of Kissinger to perform molecular replacement by following the teaching of Kissinger for a given search model). The claimed invention thus clearly provides unexpected advantages over the weak suggestion to try provided by Kissinger.

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#### CONCLUSION

Applicants earnestly believe that they are entitled to a letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent application to issuance. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

> Respectfully submitted, Takeda San Diego, Inc.

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